



Dyslipidemia & Biochemical Aspect of Atherosclerosis

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INTENDED LEARNING OBJECTIVES (ILO)



By the end of this lecture the student will be able to:

1. Correlate defects in lipoprotein metabolism to dyslipidemia.
2. Discuss the biochemical basis of atherosclerosis.

Disorders of plasma lipoproteins:

Hyperlipoproteinemia and Hypolipoproteinemia

1. Hyperlipidemia, hyperlipoproteinemia or dyslipidemia:

- is the presence of raised or abnormal levels of lipids and/or lipoproteins in the blood. The type of lipoprotein determines the fate of the particle and its influence on metabolism.
- Lipid and lipoprotein abnormalities are extremely common in the general population, and are regarded as a highly risk factor for cardiovascular disease due to the influence of cholesterol, one of the most clinically relevant lipid substances, on atherosclerosis.

Hyper-lipoproteinemia

**Primary Hyper
lipoproteinemia**

**Secondary Hyper
lipoproteinemia_**

Type I Hyperlipoproteinemia



- Due to a deficiency of lipoprotein lipase (LPL) or its activator apolipoprotein CII
- Dramatic accumulation (≥ 1000 mg/dl) of chylomicrons in plasma (chylomicronemia)
- Usually associated with acute abdomen due to acute pancreatitis
- $\uparrow$ plasma TAG even in the fasted state i.e fasting hypertriacylglycerolemia
- Creamy white plasma on taking blood sample.



Type IIa hyperlipoproteinemia or Familial hypercholesterolaemia



- The most common form.
- Mutation in the LDL receptor or the ApoB gene, resulting in increase plasma LDL level & therefore, plasma cholesterol level
- Characterized by Pre-mature atherosclerosis and increased risk for early-onset ischemic heart diseases.
- Associated with the presence of tendon xanthomas on hands and ankles



Secondary hyperlipoproteineimia



Associated with diseases as

- 1. Obesity**
- 2. Obstructive Jaundice**
- 3. DM**
- 4. Hypothyroidism**
- 5. Kidney diseases as nephrotic syndrome.**

Hypolipoproteinemia

a) **Tangier disease** ; due to failure of the liver to **synthesize Apo A and or ABCA1** . HDL is almost deficient from the plasma with accumulation of the CE in most tissues .

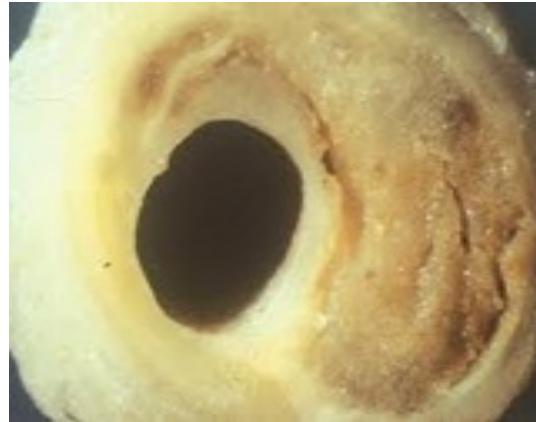
b) **Familial Abetalipoproteinemia** ; in which there is deficiency of Apo B100 . β -lipoprotein (LDL) is **abscent** from the plasma and most lipid fractions are of low concentration

c) **Familial hypobetalipoproteinemia** ;

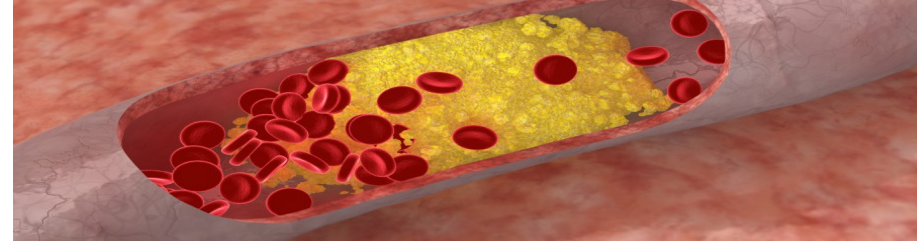
This is due to decreased synthesis of Apo B100 by the liver. So the plasma level of LDL is greatly **reduced** .



Atherosclerosis



Atherosclerosis



- Atherosclerosis is a disease affecting arterial blood vessels.
- It is a chronic inflammatory response in the walls of arteries, mostly due to the accumulation of macrophages promoted by LDL without adequate removal of cholesterol by functional HDL.
- This leads to the formation of multiple plaques within the arteries

Biochemical basis of development of atherosclerosis



- 1- Modified LDL (oxLDL: oxidized lipids and apolipoprotein) due to oxidative stress**
- 2- Uptake of oxLDL by macrophage scavenger receptor class A (SR-A) → Foam cell transformation and atherosclerotic plaque formation**





Risk factors of Atherosclerosis

1. ↑ Blood Cholesterol

- Diabetes mellitus
- Obstructive jaundice
- Familial hypercholesterolemia
- Hypothyroidism
- Nephrotic syndrome

Conditions decreasing Blood cholesterol

- Administration of estrogens
- Hyperthyroidism
- Hypocholesterolemic drugs (Statin)

Healthy, Ideal Level Lipid Profile



Fasting Blood Level

Total Cholesterol	< 200 mg/dl
LDL-Cholesterol	< 100 mg/dl
HDL-Cholesterol	≥ 60 mg/dl
Triglycerides	< 150 mg/dl

Risk factors of Atherosclerosis

2. ↓ HDL/LDL ratio ; below 0.3

↑ HDL in premenopausal women > men & postmenopausal women.

- Estrogen in women: ↓ both Total cholesterol & LDL and ↑ HDL serum levels.
1. Estrogen increases expression of LDL receptors on cell surfaces, resulting in augmented clearance of LDL from the plasma.
 2. It also increases HDL levels due to increase production of apolipoprotein A-I in liver.
 3. Estrogen also increases formation of bile acids in liver.

3. ↓ PUFA

PUFA in diet decrease the risk because it increases solubility of cholesterol

4. ↑ Sucrose and Fructose

Sucrose and fructose are atherogenic substance tend to stimulate synthesis of triacylglycerol.

5. Coffee drinking & Cigarette smoking

- **↑ lipolysis □ ↑ FFA □ ↑ plasma lipoproteins.**
- **Cigarette smoke products are oxidants and can oxidize LDL and Damages the artery wall.**
- **Cigarette smoking compromises the body's antioxidant vitamin status, especially Vit. C**

6. Obesity and Sedentary life

- **Increased VLDL Synthesis in liver due to increase cholesterol synthesis and lipogenesis, $\uparrow$ VLDL $\rightarrow$ $\uparrow$ LDL**

7. Hypertension

- **(Blood pressure $\geq 140/90$ mmHg).**
- **Damages the artery wall allowing LDL to enter the wall more readily**

8. Family History and Age

- **Family history of premature CHD in first-degree relative**
- **Age (men ≥ 45 years; women ≥ 55 years)**



Familial hypercholesterolemia (Type II) is a result of defect in:

- A- LDL receptors.**
- B- Chylomicron receptor.**
- C- Hepatic lipase.**
- D- Apo B 48.**
- E- Lipoprotein lipase.**

SUGGESTED TEXTBOOKS



1. Lippincott's illustrated reviews in Biochemistry (6th edition) p.227-237 for cholesterol and steroid metabolism.
2. National Institutes of Health (NIH) Publication No. 01-3305 May 2001 (National Heart, Lung, and Blood Institute) Adult Treatment Panel III (ATP III) guidelines included in the National Cholesterol Education Program (NCEP) report, ATP III Guidelines At-A-Glance Quick Desk Reference.

A bouquet of red roses with a red ribbon, lying on a dark, wet surface. The roses are vibrant red with green leaves, and the ribbon is a matching red. The surface is dark and reflective, with water droplets visible. The text "Thank you" is written in a large, white, italicized font in the upper right corner.

Thank you